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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/785,548 | 02/20/2001 | Hana Koutnikova | ST00005 | 5202 |

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WILEY, REIN & FIELDING, LLP
ATTN: PATENT ADMINISTRATION
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| EXAMINER |
|---|
| HAYES, ROBERT CLINTON |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | |

DATE MAILED: 02/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/785,548 | Koutnikova et al |
| **Examiner** | **Art Unit** |
| Robert C. Hayes, Ph.D. | 1647 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *Nov 27, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *32-62* is/are pending in the application.

4a) Of the above, claim(s) *43-52, 54-58, and 60-62* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *32-42, 53, and 59* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *32-62* are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *12*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Sequence Rules*

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) because 37 CFR 1.821 (a)(2)(c-d) states that *each sequence disclosed must appear separately* in the "Sequence listing" and *in the text of the description* and claims whenever described (e.g., pgs.19-20, as it relates to Figs. 6-7 & 9-10; pg. 26 (line 9); etc.). See MPEP 2422 & 2431. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) in order to be fully responsive to this Office Action.

### *Drawings*

2. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied. It is noted that 3 copies and a petition plus fee was submitted as Paper No.4.

***Election/Restriction***

3. It is noted that claim 35 uses improper Markush language. Elements within a Markush group are required to possess some structural similarity (e.g., be classified within the same class). See M.P.E.P. 2173.05(h). Appropriate correction is required.

4. Applicant's election with traverse of Group I (claims 32-42, 53 & 59; as it relates to the peptide of SEQ ID NO:2) in Paper No. 11 is acknowledged. The traversal is on the ground(s) that "at least some of the claims are related in that, for example, they encompass both methods for using the recited peptide or polypeptide and the polypeptides or peptides themselves", that "these groups of claims should be joined and examined together", cites MPEP 821.04 and 1184 O.G. 86, March 26, 1996, and states that "Paper No.10 fails to satisfy the requirement for showing a serious burden in examining the claims and even the sequences together". This is not found persuasive because the current claims are not directed toward "nucleotide sequences". *In* arguendo, MPEP 803.04 states "[n]ucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to each other", and that it "may be necessitated that the reasonable number of sequences to be selected be less than ten". In other words, one sequence is reasonable, due to the exponential growth in the number of sequences now available and required to be checked since the 1996 O.G. notice. Further, in regards to Applicants' comments for rejoining all groups, each of the products claimed can be prepared by

different processes, such as though chemical synthesis or isolation from natural sources using various isolation/purification procedures, they are physically and functionally distinct, and they can be used in different distinct methods, which themselves require different goals, starting materials, and different and unique search parameters. It is again pointed out that there is a proper distinction between these groups, since each product and/or method is not required in order for the other to exist. Therefore, the non-coextensiveness of the search and examination for each group would constitute an undue burden on the examiner to search and consider each of these separable groups, the requirement is still deemed proper, and is therefore made FINAL.

Claims 43-52, 54-58 & 60-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

***Priority***

5. This application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application. A statement reading "This application claims the benefit of U.S. Provisional Application No. 60/198,489, filed 4/18/00." should be entered following the title of the invention or as the first sentence of the specification.

### *Claim Rejections - 35 U.S.C. § 101*

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 38 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

Claim 38 recites " a peptide compound derived from the PAP1 protein..... that has been rendered nonfunctional". Thus, because this peptide compound must be "nonfunctional", no specific utility can reasonably exist; nor can a substantial utility exist.

Applicant is directed toward the Revised Interim Utility Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999.

### *Claim Rejections - 35 U.S.C. § 112*

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 38 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Claims 32-42, 53 & 59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification describes the human PAP1 polypeptide of SEQ ID NO:2, which interacts with parkin, as well as splice variants thereof (e.g., see page 4 of the specification). No PAP-1 polypeptides are described from any "other organisms"/species (e.g., as it relates to pg.5 of the specification). In other words, no adequate written description of what constitutes any different species or different open reading frame that merely "comprise" fragments of SEQ ID NO:2 is provided within the instant specification, or known in the art. The specification fails to describe what critical amino acids define any distinguishable and assayable PAP-1 function/ activity or what critical amino acid residues define "functional part of the interaction site of the PAP1 protein with parkin". Therefore, one skilled in the art cannot reasonably visualize or predict what critical amino acid residues would structurally characterize the genus of PAP-1 polypeptides, or homologs, derivatives, variants, functional parts/fragments thereof, as currently claimed; thereby, not meeting the written description requirements under 35 U.S.C. 112, first paragraph.

Applicant is directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999.

9. Claim 32-42, 53 & 59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the PAP-1 protein of SEQ ID NO:2, does not reasonably provide enablement for any biologically equivalent molecule with no structural and functional characteristics. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The name "compound capable of modulating interaction between the PAP1 protein... and parkin" or "PAP1 protein" as defined on pages 5 & 7-10 of the specification includes "homologs", "derivatives", "variants", "functional parts", "fragments", "any mutation, substitution, deletion, addition and/or modification" and biologically functional "equivalent" molecules. However, the inclusion of any random mutations within the claimed polypeptide molecules set forth no structural and no functional characteristics. In contrast, the specification fails to disclose what encoded amino acids are critical to maintaining a functional "PAP1 protein". Therefore, because the specification fails to disclose what residues can be altered and still maintain the desired functional activity of the instant invention, the resultant random mutations to this polypeptide of SEQ ID NO:2 would be predicted by the skilled artisan to result in inactive polypeptides. For example, Rudinger teaches that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence"(see page 3). Rudinger further states on page 6 that "the significance of particular

amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification, as to what alterations can be tolerated to maintain a functional PAP1 protein, would prevent the skilled artisan from determining whether any PAP1-related protein could be made that retains the desired function of the instant invention, without undue experimentation to determine otherwise.

10. Claims 32-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is ambiguous and contradictory for a particular compound to "slow, inhibit or stimulate"/ "modulate" a binding reaction. Either a compound interferes with PAP1 binding to parkin, or it does not.

11. Claim 59 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, a composition is composed of at least two components, such as a peptide and a carrier.

***Claim Rejections - 35 U.S.C. § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
>
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 32-42, 53 & 59 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al. (WO 01/46256 A2).

Tang et al teach an isolated VETRP polypeptide of SEQ ID NO:3 , which is nearly identical to the PAP1 protein of SEQ ID NO:2 of the instant invention, and "comprises" 5/9/15 consecutive resides of SEQ ID NO:2 (e.g., pgs. 7, 12, 15-16, 20, 25, 73 & 95; as it relates to claims 36 & 39-42; thereby, inherently also meeting the limitations of a "compound capable of modulating interaction between the PAP1 protein/domain... and parkin", which "slows, inhibits or stimulates said interaction". Tang's polypeptide further constitutes a homolog, derivative, variant, functional part/fragment of the polypeptide of SEQ ID NO:2, as defined by the

specification. Composition comprising Tang's polypeptides and pharmaceutically acceptable carriers are disclosed on pages 48 & 97; thereby, also meeting the limitations of claims 53 & 59.

13. Claims 32-34, 53 & 59 are rejected under 35 U.S.C. 102(b) as being anticipated by the Stratagene 1991 Product Catalog.

Stratagene Product #300071/ EDTA is a "compound capable of modulating interaction between the PAP1 protein/domain... and parkin", which inherently "slows, inhibits or stimulates said interaction", based on the disclosure on page 3 of the specification that PAP1 "binds metals" and EDTA is well known in the art to chelate metals; thereby, modulating binding reactions (i.e., pg. 95; as it relates to claims 32-34). In that the addition of the pharmaceutically acceptable vehicle/excipient, water, makes a "composition" of EDTA, the limitations of claims 53 & 59 are also met.

***Conclusion***

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
February 14, 2003

GARY KUNZ
SUPERVISORY PATENT EXAMINER
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